EXHIBIT A

Mitchell J. Banas, Jr.

From: Edmund Egan <eegan@ony.incubator.buffalo.edu>
Sent: Friday, October 14, 2011 12:08 PM
To: Ned Lawson
Subject: RE: Request for Retraction Reconsideratin
Signed By: eegan@ony.incubator.buffalo.edu

Dear Dr. Lawson,

I appreciate your detailed and thoughtful response to my concerns about paper by Ramanathan et al. However, I also request that you reconsider your decision about retraction. In re-reading my request for the retraction I may have been less than clear. It is the omission of the Length Of Stay (LOS) data that was unquestionably available to the authors for the time span used for the publication that makes the paper scientifically unreliable. Why the LOS data was omitted is irrelevant for a retraction decision. Without the LOS data the mortality differences are "unreliable" and the paper meets the criteria that requires retraction under the Guidance of the Committee for Publication Ethics.

I take issue with your assessment of the omission of the LOS data. Your assertion that "An equally valid argument would be that longer LOS following other surfactants would be due to emergence of excess BPD or other chronic effects" has **NO** scientific basis. In 30 plus years of clinical studies no surfactant has been shown to alter the incidence or severity of BPD or other chronic effects in infants <1250 grams birth weight. Possible explanations must also be consistent with facts. If the authors had included the LOS data neither you nor your reviewers would have allowed this paper to conclude that lower mortality and a shorter length of stay for Curosurf patients means that Curosurf has both a mortality benefit and lowers the incidence and/or severity of BPD or other chronic conditions compared to other products. You further commented, "Of course other possibilities exist (selection bias, prophylactic vs. rescue, etc.)." These "other possibilities" and several others included in "etc" immediately arise to a reviewer or reader if the available LOS data had been included in the paper. An assertion that the message of this paper is no more or less reliable without the LOS data does not pass the "red face test."

I unreservedly accept as subjectively true your statement "However, I would like to believe that I accepted the manuscript (despite the conflicting reviewer recommendations) based upon my opinion balancing all of the information I had at the time." No single individual remembers every abstract from every meeting. I have no complaint about your function as the editor of the original manuscript. However, The guidelines on retractions are clear, it is the reliability of the information published, not the problems or lack of problems in their pathway to publication, that mandates a retraction.

I will not comment further on whether these authors are objective scientists seeking to increase objective knowledge or have become, wittingly or unwittingly, salespersons delivering a packaged message for a commercial product. View Dr. Bhatia's "objective" discussion of Curosurf on you tube (http://www.YouTube.com/watch?v=tLpUTL1-QEw). Make your own decision. Your reliance on Dr. Bhatia's expertise perhaps should be re-assessed. Your quote him, "The paper cited by Dr. Egan published in the E Journal of Neonatal Research is an analysis of trends in surfactant use and has no bearing on mortality or the current paper." In fact the final rows of table 2 of the Trembath et al. paper presents data on bronchopulmonary dysplasia and deaths in a retrospective study of surfactant use in a population of 13,784 patients. How is that not a relevant to Dr. Bhatia's retrospective paper on differential surfactant mortality?

This is black or white issue; a paper is either reliable or unreliable. If the Journal of Perinatology does not

retract this article, especially after my communications to you and the Academy of Pediatrics, then there is the inescapable conclusion that the leadership of the journal and its sponsors endorses the reliability of the message of this paper. A reputable journal publishes (and lets stand) peer reviewed publications whose results are reliable. Uncertainty equals unreliability.

As I stated previously, retraction is the academically appropriate resolution, much superior to other options. Please advise me when you have reconsidered this.

Edmund A. (Ted) Egan, MD
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State University of New York at Buffalo
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1576 Sweet Home Road
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716-636-9096 fax 716-636-3942

n.b. I trust Dr. James Cummings will inform me of his reading of this paper if and when he judges it appropriate.

From: Ned Lawson [mailto:elawson@jhmi.edu]
Sent: Wednesday, October 12, 2011 11:56 AM
To: Edmund Egan
Cc: De Myer, Desiree; jcouto@aap.org; frank_ernst@premierinc.com; Jatinder Bhatia
Subject: RE: Request for Retraction - Hard Copy to Follow by Courier

October 12, 2011
Dear Dr. Egan

Thank you for your letter of September 22, 2011. I received both the email and hard copy versions. I sent the letter to Dr. Bhatia for his comments. Also I have read the abstracts, reread the manuscript by Ramanathan et al (J Per advanced online publication 9/1/2011), and have briefly communicated with Jim Couto, the AAP support manager for the Section on Perinatal Pediatrics of the American Academy of Pediatrics (AAP).

In my opinion, Dr. Alden is an inappropriate person to involve regarding your concerns. As Executive Director of the AAP, Dr. Alden does oversee the publications from the AAP. However, though the Journal of Perinatology is the "official Journal of the Section on Perinatal Pediatrics, American Academy of Pediatrics", it is not owned or otherwise associated with the AAP. The Journal of Perinatology is owned, published and distributed by Nature Publishing Group. My responsibility as Editor in Chief is designated through a direct connection to NPG. Hence, Dr. Alden has no actual oversight responsibility for the Journal of Perinatology. Regardless, I will send him a copy of this letter (via Mr. Couto). In the sense of complete disclosure I also report semiannually to the SoPPe Executive Board and annually to the J Perinatology Editorial Board.
In regards to the Ramanathan et al manuscript: I handled it as the Editor. It was reviewed independently by two external reviewers – one an Editorial Board Member and the other an independent reviewer. Both reviewers were positive about the article. One of the two reviewers was concerned, as you are, that all the authors have conflicts of interest related to their past activities with the commercial interests that own poractant alfa (Curosurf™). Having mediated concerns such as this I have learned that authors are offended that their scientific integrity is impugned when apparent conflicts of interest are raised as an issue to reject a manuscript. I have also noted that people having a financial stake in the alternative products are especially prone to raise the issue of "conflicted authors" when the reported data are adverse to their interests. It then falls on my shoulders to review the letters and manuscripts that are involved in these controversies and decide the degree to which the manuscripts and letters are compromised by the potential conflicts. In my opinion at

the time of deciding whether to accept or reject this particular manuscript, I decided that the potential conflicts were well identified in the manuscript. This is the accepted standard unless, as you state, there are obvious reasons to doubt the results of the study. Since I did not have significant concern for the data integrity I accepted the manuscript for publication in the Journal of Perinatology.

Regarding your concerns of data integrity: You state that the data from the abstracts conflict with those of the manuscript and this is a reason for the retraction request. First, I note that the mortality data from the PAS abstract have virtually identical OR results for the poractant alfa vs. calfactant (Infasurf™) comparisons (as is true for PA v BE, and BE v CA) as those reported in the manuscript. Second, the data from the two abstracts (PAS abstract and Acta Pediatrica abstract) and the Journal manuscript derive from different time frames (albeit overlapping). Third, I respectfully disagree that shorter length of stay inevitably indicates excess early mortality and thereby these data from the Acta Pediatrica abstract are sufficient to retract the manuscript. An equally valid argument would be that longer LOS following other surfactants would be due to emergence of excess BPD or other chronic effects. Of course other possibilities exist (selection bias, prophylactic vs. rescue, etc.).

You asked a series of specific questions to support of your request to retract this manuscript.

Regarding Question 1 – why were abstract authors dropped from the published manuscript? Dr. Bhatia answered that the abstracts and the manuscript are the result of different studies and the dropped authors were not associated with the study reported in the Journal. On my review of the data from all three reports, I note that the two abstracts report different inclusion dates and different numbers of patients and hospitals involved than the manuscript. Hence, I agree that the data reported in the two abstracts derive from an independent study and dropping non-involved authors was appropriate.

Regarding Question 2 - why was Trembath et al not referenced? Bhatia answers this as: "The paper cited by Dr. Egan published in the E Journal of Neonatal Research is an analysis of trends in surfactant use and has no bearing on mortality or the current paper. In fact, it is favorable to Curosurf and Infasurf, as stated. Further, Dr. Bloom [an author of the Tremblath study] is a paid consultant for Ony, Inc., Inc., [sic] and was a co-author."

Regarding Question 3 - You asked whether Dr. Bhatia's relation to the Journal as an Associate Editor had bearing on my decision to accept the paper. You missed the fact that Dr. Sekar is on the Editorial Board of the Journal and so two of the four authors have official relationships (to which I appointed them) with the Journal. These relationships certainly did not hurt them in my decision whether to accept or reject the manuscript. However, I would like to believe that I accepted the manuscript (despite the conflicting reviewer recommendations) based upon my opinion balancing all of the information I had at the time. I should note it is not unusual for me (or editors of other journals) to override the counsel of the external reviewers – especially when their recommendations are not congruent. Dr. Garfunkel, the Editor in Chief of the Journal of Pediatrics when I was an Associate Editor, taught me that necessity (e.g. the editor is a valid reviewer).

Regarding Question 4 - What is definition of Consultant? Dr. Bhatia answers as follows: "Drs. Ramanathan, Sekar and I were on the Advisory Board to Dey LP and were on the speakers' bureau. The Board does not exist anymore and I and Dr. Sekar ceased being on the speakers bureau a few years ago. .... Dr. Egan fails to remember that I along with Dr. deLemos and several others were on the Infasurf Advisory Board before it was launched!" Dr. Bhatia's Infrasurf conflict was not mentioned in the manuscript publication COI statement. Dr. Ernst's relationship to Chiesi is through Premier and is identified in the COI statement in the published manuscript.

Consequently, I conclude there is inadequate evidence to consider retracting the publication based upon any of the potential reasons cited in your letter.

In my first draft of my response to your letter I was going to offer you the opportunity to write a letter to the editor to identify your concerns about the Ramanathan et al paper. However, since then I have received a letter from your past colleague, James Cummings, who raises most of the very same concerns you do (abstracts, Trembath, etc). His letter is very critical of the Ramanathan paper, and his arguments are largely based upon the methods of the paper itself. I have written Dr. Cummings that his paper is acceptable for publication given

minor changes that include his signature and a Conflict of Interest statement. I have also sent that letter to Dr. Ernst – the corresponding author of the Ramanathan et al manuscript - for those authors to provide a response. I intend to co-publish both letters simultaneously in the first available print issue following acceptance of the galley proofs by their respective authors. Because Dr. Cummings' letter is so similar to your concerns, I do not believe it necessary for you, as President of ONY, Inc, the owner of Infasurf, to provide a second response. Because of your clear conflict, I believe that letting Dr. Cummings "carry the flag" in this discussion will strengthen your position. I hope you agree with this decision. A similar solution was satisfactory to a different surfactant company who strongly objected to a prior article in the Journal by a different author based largely upon their perception of conflict of interest.

Because submitted manuscripts and letters are confidential until published, I cannot share with you Dr. Cummings' letter. However, since you two were prior colleagues I believe he would be willing to share his letter with you. Also, I will not send a copy of this letter to Dr. Cummings. I usually copy letters to people mentioned in my correspondence, but in this case I will keep my letter confidential to you, unless you decide to share it with Dr. Cummings.

Yours

Ned

Edward E. Lawson, MD
Editor-in-Chief
Journal of Perinatology

Cc
Jim Couto for Errol Alden, MD
Frank Ernst, PharmD
Jatinder Bhatia, MBBS
Desiree de Myer, NPG Managing Editor, J Perinatology

From: Edmund Egan [mailto:eegan@ony.incubator.buffalo.edu]
Sent: Thursday, September 22, 2011 4:56 PM
To: Ned Lawson; ealden@aap.org
Subject: Request for Retraction - Hard Copy to Follow by Courier

Errol Alden, MD
Executive Director
American Academy of Pediatrics
141 Northwest Point Blvd
Elk Grove Village, IL 60007-1019

Edward E. Lawson, MD
Editor, Journal of Perinatology
600 N Wolfe St Nelson 2-133
Baltimore, MD 21287-0001

RE: *Ramanathan R, Bhatia JJ, Sekar K, Ernst FR. Mortality in preterm infants with respiratory distress syndrome treated with poractant alfa, calfactant or beractant: a retrospective study. Journal of Perinatology (2011) Pages 1-7 e-published September 1, 2011.*

Dear Drs. Alden and Lawson,

I am writing on behalf of ONY, Inc. the owner of Infasurf, and contacting the two of you about the above article because Dr. Alden is the responsible officer for the sponsoring organization of the Journal of Perinatology and Dr. Lawson is the editor of the Journal of Perinatology. I am requesting that the above article be retracted because the sponsoring company with, or without, the active participation of the listed authors have published partial data to provide Chiesi Farmaceutici SpA with an "Infomercial" disguised as a peer reviewed publication.

This is not a new study. It has been available and published as abstracts several years ago (see abstracts at the end of this communication). The abstract presented at the Pediatric Academic Societies meeting in Toronto in 2007 identifies a lower Curosurf mortality. The abstract published in Acta Paediatrica in 2007 identifies the same data base as showing a shorter length of stay for Curosurf patients. Taken together these two abstracts provide data that refutes the contention of the paper e-published this month in the Journal of Perinatology. The two abstracts report that patients treated with Curosurf not only had a lower mortality but shorter lengths of stay than those treated with Infasurf or Survanta. If treatment with Curosurf was saving lives of neonatal patients who would have died had they been treated with Infasurf or Survanta, it would have produced a longer length of stay, not a shorter one. Preventing death from RDS turns short hospital stays (early neonatal deaths) into long hospital stays (surviving and hospitalized until old enough for discharge). A shorter length of stay and the lower mortality is only compatible with the Curosurf group being less ill and a lower mortality risk than the Infasurf or Survanta groups. Omitting the length of stay data from the "peer reviewed" publication is incompatible with real science. The sponsor of the study wanted a certain result published, not an honest scientific evaluation of the issue. That is why I am insisting that the paper be retracted.

I have further scientific and ethical concerns with this paper.

1. Why were the authors included on the abstracts who were from marketing companies not included as authors on the Journal of Perinatology article? Intellectual honesty demands that all of those who were involved in generating the "research" are required to be identified.
2. Why was a similar article published 6 months ago with an entirely different result neither referenced nor discussed (Trembath AN, Clark RH, Bloom BT, Smith PB, Bose C, Laughon M. Trends in surfactant use in the United States: changes in clinical practice. E Journal of Neonatal Research, 2011; 1:23-30.).
3. Is the fact that Dr. Bhatia who is an author of this paper and the Associate Editor for Supplements of the Journal of Perinatology the reason that a paper such as this is accepted?
4. What is the definition of consultant, the term used to identify the relationship of Chiesi Farmaceutici SpA and the authors? The public relationship of Dr. Ramanathan and Bhatia and Chiesi Farmaceutici SpA is long term and multifaceted. Their public activity can be fairly characterized as promoters of Curosurf, not merely consultants to Chiesi Farmaceutici SpA. What the non-public relationships are I, obviously, do not know.

The document Retractions: Guidance from the Committee on Publication Ethics, an organization which lists the Journal of Perinatology as a member, identifies which publications should be retracted (http://publicationethics.org/files/u661/Retractions_COPE_gline_final_3_Sept_09__2_.pdf)
That Guidance states in its Summary, "*Journal editors should consider retracting a publication if they have clear evidence that the findings are unreliable, either as a result of misconduct (e.g. data fabrication) or honest error (e.g. miscalculation or experimental error)*" Later in the document in its discussion of which publications should be retracted it states retraction is appropriate in the case of. "*...publications that are so seriously flawed (for whatever reason) that their findings or conclusions should not be relied upon.*" I have requested a retraction because data the authors themselves have previously made public in abstracts prove that this publication's findings are unreliable, seriously flawed and should not be relied upon.

Pharmaceutical companies that are committed to using peer reviewed publications to inform the physician community about the science of their products are as poorly served as the physician community when non-science such as this is published in a peer reviewed journal. The Curosurf website touts this article: "*Overall*

Curosurf treatment for RDS was associated with a significantly reduced likelihood of death compared to Infasurf and a trend toward reduced mortality compared to when compared with Survanta." Cornerstone Therapeutics, the United States company marketing Curosurf , will widely disseminate this publication to busy neonatal practitioners who rely on the integrity of the Academy of Pediatrics and the journals it sponsors to insure that the papers published are scientifically valid. This paper betrays that trust.

Retraction is the appropriate and optimal course for the Journal of Perinatology, the Academy of Pediatrics and neonatology community. Other options to rectify this problem entail collateral effects that make them less desirable.

Sincerely,

Edmund A. Egan, MD
Professor of Pediatrics and Physiology & Biophysics
State University of New York at Buffalo
President, ONY, Inc.

[7935.16] Differences in Mortality among infants Treated with Three Different Natural Surfactants for Respiratory Distress Syndrome.

J. Bhatia, W.B. Sunders, P. Friedlich, P.T. Levin, K.C> Sekar, J.M. York, R. Ramanathan. Neonatology, Medical College of Georgia, Augusta, GA; Analytics and Research, Premier, Inc. Charlotte, NC; Neonatology, Women and Children's Hospital, Los Angeles, CA; Averion Corporation, Southborough, MA; Neonatology, University of Oklahoma Health Science Center, Oklahoma City, OK; Akita Biomedical Consulting, San Clemente, CA.

BACKGROUND: Observations from a previous randomized, comparative surfactant clinical trial suggest an association between the type of surfactant used and neonatal mortality.
OBJECTIVE: To determine mortality differences in neonates with respiratory distress syndrome (RDS) treated with poractant alfa (PA) *versus* beractant (BE) and calfactant (CA), using a defined database which was independently collected and analyzed.
DESIGN/METHODS: Data were analyzed from 191 hospitals between January 2003 and June 2006 using Premier's Perspective™ hospital-based, clinical database. Cohort selection included neonates ICD-9 coded for RDS and treated with PA, BE or CA. Multivariate logistic regression analysis was used to compare in-hospital all cause mortality while controlling for case mix and the following covariates: birthweight gestation age (GA) race, gender, and transfer status. Case-weighting models were evaluated for all infants plus a subset with complete patient data. The impact of the missing data (primarily GA) was evaluated to test for selection bias.
RESULTS: Data were analyzed from 24907 infants in the total cohort (TC) and a subset cohort (SC) of 10,237 with complete data (See Table with odds rations, OR). Mortality in the PS cohort was lower *vs* BE and CA for all covariates in both models, ($p<0.001$), except for missing GA data in the TC model ($p=0.94$).

Unadjusted Mortality % and Adjusted OR (95% CI) for TC and SC

Surfactant Type	PA	BE	CA
TC RDS treated infants (n)	4,986	12,674	7,277
TC unadjusted mortality %	6.25	8.15	8.31
TC adj OR (95% CI)		1.28* (1.20-1.36)	1.47* (1.37-1.58)
SC RDS treated infants (n)	2,191	5,248	2,798
SC Adj OR (95% CI)		1.52** (1.32-1.70)	1.60** (1.41-1.82)

* Mortality for PA vs BE was 22% lower; and 32% lower vs CA. ***Mortality for PA vs BE was 34% lower and 37% lower vs CA. P<0.001 for both results.

CONCLUSIONS: Analysis of a large, clinical database, using a diagnosis of RDS in premature infants indicates that treatment with PA is associated with lower mortality than BE or CA. (Funded by Dey, LP and Chiesi Farmaceutici SpA)

E-PAS2007:617935.16

Monday, May 7, 2007 3:00 PM

Poster Session: Neonatology (3:00 PM – 6:45 PM)
Board Number: 490
Course Number 7935

Acta Pediatr 2007; 96 Suppl 456, p109 (Abstract)

Resource use in pre term neonates with respiratory distress syndrome (RDS) treated with one of three different natural surfactants: analyses using a large hospital discharge database

K C Sekar[1], J Bhatia[2], F R Ernst[3], W B Saunders[3], P T Lavin[4], R Ramanathan[5]

[1].University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [2]. Medical College of Georgia, Augusta, GA, USA; [3].PremierResearchServices, Premier Inc, Charlotte, NC, USA; [4].Averion International Corporation, Southborough, MA, USA; [5].Women's and Children's Hospital, Los Angeles, CA, USA

Background and aims: Surfactant treatment for respiratory distress syndrome (RDS) reduces morbidity and length of stay (LOS) in pre term neonates. In a previous cost minimization analysis, poractant alfa (PA) was found to be more cost effective than beractant (BE) due to decreased need for additional doses. However, there are no cost analysis data comparing natural surfactants with respect to the total cost of neonatal care, including LOS. Our objectives were to assess differences in hospital and neonatal ICU (NICU) LOS, and total hospital costs among neonates with RDS treated with PA, BE, or calfactant (CA).

Methods: Neonatal cohort data (n = 24 883) collected from 191 hospitals using Premier's Perspective TM data set from January 2003 to June 2006 were analyzed. This cohort included pre term neonates with RDS treated with a single surfactant: PA, BE, or CA. Non-parametric testing (Wilcoxon rank sum) was used to determine differences in median NICU and hospital LOS, and total hospital costs. Actual hospital costs incurred were used in this analysis.

Results: Median hospital LOS and NICU LOS were 21 and 17 days in PA group, as compared to 25 and 20 in BE and 30 and 21 in CA (PA versus BE or CA: both $P < 0.0001$). Median hospital costs were $26 715 in PA group as compared to $31 199 in BE and $36 652 in CA (both $P < 0.0001$). Conclusions: Pre-term neonates with RDS treated with PA demonstrated significant reductions in hospital and NICU LOS, and total hospital costs when compared with BA and CA. (Funded by Dey, LP and Chiesi Farmaceutici, SpA.).